



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/711,101	08/23/2004	George Blanck	1372.183.PRC	5100
21901	7590	12/22/2008		
SMITH HOPEN, PA 180 PINE AVENUE NORTH OLDSMAR, FL 34677			EXAMINER VIVLEMORE, TRACY ANN	
			ART UNIT	PAPER NUMBER
			1635	
			MAIL DATE	DELIVERY MODE
			12/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte GEORGE BLANCK, KIMBERLY PALUBIN and AARON
OSBORNE

Appeal 2008-5485
Application 10/711,101
Technology Center 1600

Decided: December 22, 2008

Before ERIC GRIMES, RICHARD M. LEOVITZ, and STEPHEN
WALSH, *Administrative Patent Judges*.

WALSH, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method for treating a tumor. The Examiner rejected the claims as lacking written description and enablement. We have jurisdiction under 35 U.S.C. § 6(b). We affirm-in-part and reverse-in-part.

STATEMENT OF THE CASE

Appellants claim a method for treating a tumor in a patient comprising administering a therapeutically effective amount of an Oct-1 inhibitor. The Examiner required restriction between a method that inhibits Oct-1 binding

activity (Claims 9 and 10) and a method that inhibits Oct-1 mRNA function (Claims 9 and 11-13). (Office communication mailed 8/28/2006, designating Claim 9 as a “linking claim”). Appellants elected the method that inhibits Oct-1 mRNA function for examination. (Paper filed 9/27/2006.) Claim 10 was accordingly withdrawn from examination.¹ (Ans. 2.)

Claims 9 and 11-13 are on appeal. The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Claim 11 is representative of the subject matter elected for examination. Claims 9 and 11 read:

9. A method for treating a tumor in a subject in need thereof, comprising administering a therapeutically effective amount of an Oct-1 inhibitor.
11. The method of claim 9 wherein an Oct-1 inhibitor inhibits Oct-1 mRNA function.

The Examiner rejected the claims as follows:

- Claims 9 and 11 are rejected under 35 U.S.C. § 112, first paragraph, for failure to comply with the written description requirement;
- Claims 9 and 11-13 are rejected under 35 U.S.C. § 112, first paragraph, for failure to comply with the enablement requirement.

¹ Claims 4-8 are also pending but withdrawn from consideration as a result of an earlier restriction requirement and election. (Office action mailed 2/2/2006.)

WRITTEN DESCRIPTION

The Examiner rejected claims 9 and 11 under 35 U.S.C. § 112, first paragraph, as lacking written description support. The Examiner's position is that the claims encompass the use of inhibitors of Oct-1 mRNA function "of any type," including both nucleic acid-based inhibitors and "non-nucleic acid inhibitors such as proteins, antibodies, small organic molecules and inorganic molecules." (Ans. 4.) The Specification disclosed using an antisense oligonucleotide, but the Examiner found that antisense inhibitors are not representative of non-nucleic acid inhibitors. (Ans. 5.) The Examiner found no description for non-nucleic acid inhibitors of Oct-1 mRNA function. Although the Examiner found that two non-nucleic acid inhibitors of Oct-1 were known in the art, the Examiner stated that the skilled artisan "cannot envision the detailed structure of the encompassed modulating agents that inhibit Oct-1 mRNA function." (Ans. 6.)

Appellants contend that the absence of a working example is not fatal to compliance with the written description requirement when the Specification otherwise conveys possession of the invention. (App. Br. 10.) A Specification may contain a written description of a broadly claimed invention without describing all the species that the claim encompasses. *Id.* "[T]he mere fact that the specification fails to describe the full genus of encompassed compounds that have the function of inhibiting OCT-1 does not mean that the application fails to meet the written description requirement." *Id.*

The issue with respect to this rejection is whether those of skill in the art would have credited Appellants with possession of the genus of Oct-1 inhibitors that inhibit Oct-1 mRNA function.

Findings of Fact Relating to the Written Description Issue

1. Oct-1 is a protein transcription factor. (Spec. ¶ 9.)
2. Oct-1 mRNA is the messenger RNA that codes for the Oct-1 protein.
3. The claimed method requires administration of “an Oct-1 inhibitor that inhibits Oct-1 mRNA function.” (App. Br. 16.)
4. One full-length antisense molecule that inhibits Oct-1 mRNA function is disclosed. (Spec. ¶ 24.)
5. The Specification does not identify or provide structural information about non-nucleic acid inhibitors of Oct-1 mRNA function.
6. Heparan sulfate and interferon α are known inhibitors of Oct-1. (Ans. 5.)
7. Appellants do not assert that heparan sulfate or interferon α inhibits Oct-1 mRNA function.
8. Appellants do not identify evidence that pre-existing knowledge in the art supplements the Specification with a description for non-nucleic acid inhibitors of Oct-1 mRNA function.

Principles of Law Relating to Written Description

When an Applicant claims a class, the Applicant “must describe that class in order to meet the description requirement of the statute.” *In re Lukach*, 442 F.2d 967, 968 (CCPA 1971). In assessing whether the written description requirement is satisfied, “[t]he primary consideration is *factual* and depends on the nature of the invention and the amount of knowledge

imparted to those skilled in the art by the disclosure.” *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562 (Fed. Cir. 1991) (citation omitted, emphasis in original). The amount of description needed to meet the requirement can vary with the scientific and technologic knowledge already in existence. *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005).

Analysis of the Written Description Issue

We construe the claim phrase “[a]n Oct-1 inhibitor that inhibits Oct-1 mRNA function” to name a genus by naming a function. The genus includes molecules or agents that function as an Oct-1 mRNA inhibitor. We agree with the Examiner’s undisputed finding that the named inhibitor genus includes both agents that have a nucleic acid structure and agents that have a non-nucleic acid structure. (Ans. 4.) The genus is “highly variant” (Ans. 6), potentially including “non-nucleic acid inhibitors such as proteins, antibodies, small organic molecules and inorganic molecules.” (Ans. 4.) The Specification does not name or provide a structural description for non-nucleic acid inhibitors of Oct-1 mRNA function (FF5), and the Examiner found that their identity and structure is not readily predictable. Appellants do not dispute those findings. We accordingly find that the burden was properly shifted to Appellants rebut the Examiner’s finding with evidence or argument. *Hyatt v. Dudas*, 492 F.3d 1365, 1370 (Fed. Cir. 2007). Rather than cite where the missing information could be found, or make an

amendment to address the deficiency, Appellants present arguments.² We address each in turn.

First, Appellants correctly observe that the absence of a working example is not fatal where the Specification otherwise conveys that the Applicants possessed the claimed invention at the time of filing. (App. Br. 10.) The Examiner acknowledged the disclosure of one working example using a nucleic acid-based Oct-1 mRNA function inhibitor, a full-length antisense molecule. The Examiner withdrew the rejections of claims using inhibitors that have a nucleic acid structure, i.e., Claim 12 (“an Oct-1 antisense sequence”) and Claim 13 (“an RNA inhibitor molecule”). (Ans. 3.)

Appellants do not indicate or explain how an inhibitor that has a nucleic acid structure is representative of non-nucleic acid structures such as proteins, antibodies, small organic molecules and inorganic molecules. There is no working example of a non-nucleic acid based Oct-1 mRNA function inhibitor, and the question is whether some other form of disclosure identifies or describes that kind of inhibitor. Appellants do not point to any evidence in the record that those of skill in the art would know of any such inhibitors. Unlike the disclosure of a single antisense molecule, which may be representative of other nucleic acid molecules such as those in Claims 12 and 13, we find no disclosure of anything representative of non-nucleic acid Oct-1 mRNA function inhibitors such as proteins, antibodies, small organic

² We do not agree with Appellants’ characterization “nor does the Examiner dispute the existence of numerous other Oct-1 inhibitors.” (App. Br. 9.) The Examiner does dispute it. (Ans. 9.)

molecules and inorganic molecules. Not only is a working example for non-nucleic acid based inhibitors absent, the Specification does not otherwise convey possession of that kind of inhibitor.

Appellants correctly observe that a specification may contain a written description of a broadly claimed invention without describing all the species that the claim encompasses, citing *Utter v. Hiraga*, 845 F.2d 993, 998 (Fed. Cir. 1988). (App. Br. 10.) In *Utter*, specific references to knowledge in the prior art supplemented the specification's limited disclosure. There, the disputed application disclosed the geometry of an internal pivot embodiment and cited prior art patents that were directed to external pivot embodiments. *Utter*, 845 F.2d at 998-99. In other words, the Specification "otherwise" conveyed possession of external pivot embodiments. The court found the disclosure that included citations to known external pivots supported a generic interference count covering both internal and external pivot embodiments. *Utter*, 845 F.2d at 999.

Unlike the party in *Utter*, Appellants have not provided citations to prior art disclosures of inhibitors that inhibit Oct-1 mRNA function. Nor did Appellants cite evidence that the two known Oct-1 inhibitors the Examiner identified (heparan sulfate and interferon α) would be recognized by those of skill in the art as inhibitors of Oct-1 mRNA function. The amount of description needed to meet the written description requirement can vary with the scientific and technologic knowledge already in existence. *Capon*, 418 F.3d at 1357. In this case, however, Appellants have not shown evidence of pre-existing knowledge relating to non-nucleic acid Oct-1 inhibiting molecules that inhibit Oct-1 mRNA function. The written description

requirement may alternatively be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a known structure. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332 (Fed. Cir. 2003). However, Appellants have not shown there was a known correlation of non-nucleic acid inhibitor structure to the function of inhibiting Oct-1 mRNA function, nor have Appellants pointed to such a correlation disclosed in their Specification.

On this record, the only known or disclosed inhibitors of Oct-1 mRNA function have a nucleic acid structure, e.g., an antisense molecule. Appellants have not shown that those of skill in the art would recognize non-nucleic acid inhibitors from that disclosure, or think that Appellants were in possession of non-nucleic acid inhibitors. Nor have Appellants shown that those of skill in the art would accept that the disclosure of nucleic acid molecules that inhibit Oct-1 mRNA function is a disclosure of non-nucleic acid molecules that inhibit Oct-1 mRNA function. “[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated.” *Noelle v. Lederman*, 355 F.3d 1343, 1350 (Fed. Cir. 2004). Appellants have not shown reversible error in the Examiner’s finding that non-nucleic acid inhibitors of Oct-1 mRNA function lack written description.

ENABLEMENT

The Examiner rejected claims 9 and 11-13 under 35 U.S.C. § 112, first paragraph, for lack of an enabling disclosure. The Examiner's position is that delivering a therapeutically effective amount of nucleic acid to an in vivo target cell is problematic, and would require more guidance than provided in the Specification or the art of record. (Ans. 7-8.) The Examiner relied on the Opalinska³ review article as evidence that using nucleic acid molecules for in vivo therapy is wanting in reliability. (Ans. 7.) While "the specification is enabling for inhibition of Oct-1 mRNA in cells *in vitro*, the specification is not enabling for . . . treating tumors in a subject . . . as the art of inhibiting gene expression by introducing oligonucleotides into an organism is neither routine nor predictable." (Ans. 8.)

Appellants contend that the Examiner relied on a per se rule rather than giving case-specific reasons; that Appellants gave precise details about the structural and chemical properties of the Oct-1 mechanism; that inhibitors of Oct-1 are detailed by functional characteristics coupled with the known correlation between Oct-1 function and structure; that numerous inhibitors of Oct-1 are known; and that one could routinely apply Appellants' techniques to inhibit Oct-1 without undue experimentation. (App. Br. 12.)

³ Joanna B. Opalinska and Alan M. Gewirtz, *Nucleic-acid Therapeutics: Basic Principles And Recent Applications*, 1 NATURE REVIEWS DRUG DISCOVERY 503-14, July 2002.

The issue with respect to this rejection is whether inefficiency and unreliability of oligonucleotide delivery to targeted cells mean that undue experimentation would have been required to use the invention.

Further Findings of Fact Related to the Enablement Issue

9. The cell line 5637 was transfected *in vitro* with a full length, antisense Oct-1 cDNA. (Spec. ¶¶ 24-28.)
10. Loss of oncogenic characteristics in the Oct-1 antisense transformants suggests that Oct-1 is a candidate oncoprotein. (Spec. ¶ 31.)
11. The Specification states: “It is within the scope of the present invention that other modes of inhibiting or eliminating Oct-1 protein, DNA or RNA expression, or DNA-binding capacity can be easily practiced by one of ordinary skill in the art. . . . Thus, it would be understood by one of ordinary skill in the art that methods to prevent cellular proliferation or tumorigenesis can be practiced by using Oct-1 RNA, DNA, cDNA, or protein molecules in such applications.” (Spec. ¶ 32.)
12. The Examiner relied on the Opalinska review article as evidence of the state of the art. (Ans. 7.)
13. Opalinska “reviews different strategies for modulating gene expression, and discusses the successes and problems that are associated with this type of therapy.” (Opalinska, 503, abstract.)
14. According to Opalinska, the prospect of using nucleic acid molecules for therapy “remains tantalizing but uncertain.” (Opalinska, 503, left col.)

15. Opalinska discusses methods that focus on destabilizing mRNA.
(Opalinska 504, right col. – 506, right col.)
16. Opalinska provides a summary of recent clinical trials with nucleic-acid drugs. (Opalinska, 508, Table 1.)
17. Opalinska's Table 1 reports on nine cancer trials targeting PKC- α , BCL2, h-RAS, or c-RAF kinase, by administering an antisense molecule. (Opalinska 508, Table 1.)
18. In trials targeting BCL2, there were two complete remissions, two partial remissions, five minor responses, and two decreases in PSA, among 61 patients treated. (Opalinska 508, Table 1.)
19. In trials targeting PKC, there were two complete remissions and 3 responses among 57 patients treated (Opalinska 508, Table 1), and "antitumor effects were modest at best." (Opalinska 509, right col.)
20. In a trial targeting h-RAS, "[f]our [out of 23] patients had stabilized disease for 6-10 cycles of treatment." (Opalinska 509, right col.)
21. In trials targeting c-RAF kinase, "[n]o major tumour responses were documented, but some patients had stabilization of their disease." (Opalinska 510, left col.)
22. According to Opalinska, the ability of nucleic acid molecules to modify gene expression in vivo is quite variable and wanting in reliability. (Opalinska 511, left col.)
23. According to Opalinska, one of the "root cause[s]" of the reliability problem is "molecule delivery to targeted cells" (Opalinska 511, left col.); "[a]nother problem in this field is the limited ability to deliver nucleic acids into cells and have them reach their target. Without this

- ability, it is clear that even an appropriately targeted sequence is not likely to be efficient.” (Opalinska, 511, right col.)
24. Opalinska’s Table 2 is entitled “Current and planned clinical trials with antisense oligonucleotides and ribozymes,” and includes Phase II and Phase III trials targeting tumors. (Opalinska, 511, Table 2.)
25. According to Opalinska, “[d]elivery technologies continue to improve, so it is likely that present methods, and/or other evolving technologies, will be used successfully to deliver optimized nucleic acids to their cellular targets. Indeed, it is our hypothesis that development of effectively targeted and efficiently delivered nucleic-acid molecules will lead to important advances in the diagnosis and treatment of human malignancies, and other diseases for which this class of molecule has been proposed to be effective.” (Opalinska, 511-12.)
26. According to Opalinska, “clinical development of antisense compounds has proceeded to the point at which several nucleic-acid drugs have entered Phase I/II, and in a few cases, Phase III trials.” (Opalinska, 512, right col.)

Principles of Law Relating to Enablement

The first paragraph of 35 U.S.C. § 112 requires that the specification teach persons skilled in the art to use the invention without undue experimentation. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). The specification must teach more than a plan for those of skill in the art to experiment at practicing the invention; it must provide sufficient guidance or specificity as to how to execute the plan. *Enzo Biochem, Inc. v. Calgene*,

Inc., 188 F.3d 1362, 1374 (Fed. Cir. 1999). The factors listed in the *Wands* case may be taken into account but not all the factors need to be reviewed.⁴ *Id.* at 1374.

Analysis of the Enablement Issue

We first address the disputed claim construction. The claims recite administering a “therapeutically effective amount of an Oct-1 inhibitor [wherein the Oct-1 inhibitor inhibits mRNA function].” Appellants argue that problems achieving a therapeutic effect need not be overcome because administering an inhibitor is all that is required. (App. Br. 15.) That is, the claims should be read as if the express limitation “therapeutically effective amount of” were not there. We decline to read “therapeutically effective amount” out of the claims and we hold the claims require that a therapeutically effective amount be administered. *See Texas Instruments Inc. v. U.S. Int’l Trade Comm’n*, 988 F.2d 1165, 1171 (Fed. Cir. 1993) (“[T]o construe the claims in the manner suggested by TI would read an express limitation out of the claims. This we will not do because courts can neither broaden nor narrow claims to give the patentee something different than what he has set forth.” (Internal quotation omitted)). Further, our reviewing court rejected a similar argument concerning a claim that read, in part, “method of ‘treating a subject in cardiac arrest’ [comprising] . . . an oxygen-

⁴ The *Wands* factors are (1) the quantity of experimentation necessary to practice the invention, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Wands*, 858 F.2d at 737.

carrying protective solution in an amount effective to deliver oxygen.” *See Manning v. Paradis*, 296 F.3d 1098, 1102-03 (Fed. Cir. 2002) (affirming Board’s construction requiring “oxygen sufficient to have a therapeutic effect”) (original emphasis deleted). As in *Manning*, we will treat “therapeutically effective” as a meaningful claim limitation. Appellants also argue that the Examiner thinks “therapeutically effective amount” is enabled. (App. Br. 15.) That is the opposite of what the Examiner said. The Examiner concluded that no therapeutic response was enabled, without quibbling about how an effective amount would be determined if, hypothetically, the method were enabled. (Ans. 14-15.)

There is a second preliminary matter: Appellants focus several arguments on inhibitors of the Oct-1 protein, rather than on inhibitors of Oct-1 mRNA function, the subject matter elected for examination. The misdirected contentions include: (1) that precise detail about the structural and chemical properties of the Oct-1 mechanism was provided, (2) that inhibitors of Oct-1 are detailed by their functional characteristics coupled with the known correlation between Oct-1 function and structure, (3) that the Examiner’s action argues that numerous inhibitors of Oct-1 are known,⁵ and (4) that the references cited by the Examiner show that Oct-1 inhibiting substances are sufficiently well-known that one could routinely apply Appellants’ techniques to inhibit Oct-1 without undue experimentation.

⁵ The Examiner did not agree that numerous Oct-1 inhibitors are known, but even if they were, the rejection is based on the unreliability and unpredictability of achieving a therapeutic effect by administering nucleic acid inhibitors of gene expression in vivo.

(App. Br. 12.) These arguments about inhibiting protein functions are not germane to delivering inhibitors of mRNA function to tumor cells, the issue raised by the Examiner.

The Examiner identified delivery to targeted cells as the significant unsolved problem for methods that administer nucleic acid molecules, citing Opalinska as evidencing the state of the art. (FF12.) The state of the art is that in vivo delivery to tumor cells is inefficient. (FF23.) The Specification gives no guidance that addresses the delivery problem, and relies on the pre-existing knowledge in the art. (FF11.) According to the Examiner, the Specification leaves the person of skill in the art to carry out trial and error experimentation. (Ans. 9.) Opalinska reported that “[d]elivery technologies continue to improve, so it is likely that present methods, and/or other evolving technologies, will be used successfully to deliver optimized nucleic acids to their targets. Indeed, it is our hypothesis that development of effectively targeted and efficiently delivered nucleic-acid molecules will lead to . . . treatment of human malignancies.” (FF25.) In the trials Opalinska reported on, the therapeutic effectiveness of methods treating cancer with antisense molecules was statistically low. (FF17-21.) That is, remissions were reported for all four of the cancer molecules targeted, but the number of patients experiencing remission of any kind was low.

Based on the evidence of record, we conclude that those of skill in the art would have expected similar results if they followed Appellants’ instruction to target Oct-1 mRNA using the methods available in the art as of the filing date. A similar degree of “therapeutically effective” results would likely have been expected. On this record, that kind and degree of result was

relied on in the art to commence not only the Phase I and II trials reported in Opalinska's Table I, but also Phase III trials as listed by Opalinska in Table 2. (FF24 and 26.) The degree of experimentation that is considered "undue" varies between different fields of endeavor and the evidence of record shows that considerable experimentation is expected in the field of the present invention.

We do not see evidence in the record that Oct-1 targeting would have required trial and error experimentation to achieve the degree of therapeutically effective results reported in Opalinska. Appellants were apparently the first to show that targeting Oct-1 mRNA function with an antisense molecule decreased cell proliferation *in vitro*. There is no Oct-1-specific evidence in the record that leads us to expect results differing from those achieved by targeting other cancer molecules *in vivo*.

CONCLUSIONS OF LAW

Those of skill in the art would not have credited Appellants with possession of the genus "Oct-1 inhibitors that inhibit Oct-1 mRNA function."

Undue experimentation would not have been required to use *in vivo* embodiments of the invention.

ORDER

The rejection of Claims 9 and 11 for lack of written description is

AFFIRMED; and

the rejection of Claims 9 and 11-13 for lack of an enabling disclosure is

REVERSED.

Appeal 2008-5485
Application 10/711,101

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED-IN-PART

Ssc:

SMITH HOPEN, PA
180 PINE AVENUE NORTH
OLDSMAR, FL 34677